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Supplementary Material to "Safety and Efficacy of Elosulfase Alfa in Australian Patients with Morquio A Syndrome: A Phase 3b Study"

Supplementary file 1. Schedule of safety and efficacy assessments

	Screening	Baseline	Treatment visit (weekly)	Efficacy assessment visits initial phase		Early termination visit
Assessments	Week -4	Week 1, Day -1	Week 2-48	Week 25	Week 49	
Clinical laboratory tests[a]	x	x		x	x	x
Immunogenicity tests[b]		x		x	x	x
Pregnancy test[c]		x		x	x	
Cervical spine imaging[d]	x				x	x
Adverse event assessment[e]	x	x	x	x	x	x
Vital signs[f]	x	x	x	x	x	x
Pulse oximetry[g]	x	x	x	x	x	x
Physical examination	x	x	x	x	x	x
Anthropometric measurements[h]		x		x	x	x
Urine KS and creatinine		x		x	x	x
6MWT[i]		xx		xx	xx	xx
3MSCT[i]		xx		xx	xx	xx
Pulmonary function tests[j]		x		x	x	x
ECG[k]	x	x		x	x	x
Sleep apnea test (when applicable)[l]		x		x	x	x
QoL (PedsQL or SF-36)[m]		x		x	x	x
Pain (APPT)		x		x	x	x

[a] Clinical laboratory tests included hematology, chemistry, and urinalysis. Laboratory samples were collected prior to dosing of study drug

[b]Blood samples for total antibodies (TAb) and neutralizing antibodies (NAb) were collected at baseline, week 25, and at week 49 or at the early withdrawal visit. NAb were not measured if TAb were negative. Samples for total IgE were collected at baseline and only analyzed if patients experienced a severe infusion associated reaction (IAR), an IAR requiring cessation of infusion, anaphylaxis or a serious hypersensitivity event, shortly after cessation of the infusion. In this case additional blood samples for total IgE and drug-specific IgE testing were also collected

[c]For women of childbearing potential only, urine pregnancy tests were performed every 24 weeks and at any visit in which pregnancy status was in question. Results of the test had to be negative to continue treatment

[d]Cervical spine imaging was performed at screening either with cervical spine (flexion-extension) radiographs to detect evidence of vertebral subluxation, or with a cervical spine magnetic resonance imaging (MRI) or computed tomography (CT) scan to detect cervical instability and spinal cord compression. In a patient without signs and symptoms of spinal cord compression, a radiograph or MRI or CT scan of the cervical spine performed within the 12 months prior to screening could be used to satisfy this criterion. Whichever method was used at screening had to remain consistent throughout the study

[e]The site had to follow-up with the patient by phone 48 hours post-infusion to assess patient health status. Adverse events were reported starting after informed consent was obtained and through 30 days after the last study visit or the last drug infusion, whichever came first.

[f]Vital signs include heart rate and blood pressure. On infusion days, vital signs were measured immediately (<30 minutes) before the infusion, every 30 minutes for the first hour of infusion, every hour for the remainder of the infusion, and immediately (<30 minutes) after the infusion

[g]On infusion days, patients were monitored by continuous pulse oximetry during infusion and for at least 60 min after infusion was completed

[h]Standing height, length, sitting height, knee height (as clinically indicated), head circumference, and weight

[i]The 6-minute walk test (6MWT) and the 3-minute stair climb test (3MSCT) were performed in duplicate in patients >5 years of age on separate days in the 5-day period prior to the study-drug infusion in the following order: 6MWT, 3MSCT, 6MWT, 3MSCT

[j]Forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), maximum voluntary ventilation (MVV), and forced inspiratory vital capacity (FIVC) were assessed in patients >7 years of age

[k]An electrocardiogram (ECG) performed within 3 months prior to screening could be used for the screening ECG

[l]As clinically indicated, some patients may have been screened for sleep apnea using pulse oximetry and then followed up with inpatient sleep study if overnight pulse oximetry was abnormal.

[m]The Pediatric Quality of Life Inventory (PedsQL) was used to assess quality of life (QoL) in children;the Short Form 36 (SF -36) was used in adults

APPT: Adolescent Pediatric Pain Tool

KS: keratan sulfate